

ROTAVIRUS AS A CAUSE OF SEVERE GASTROENTERITIS IN ADULTS

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OBJECTIVE : To determine the role of rotavirus in adults in Thailand.

BACKGROUND : Rotavirus was identified as the only etiologic agent in five percent (28/526) of adults with diarrhea who were admitted to Bamrasnaradura Hospital in Nonthaburi, Thailand during a one year period. Infection was determined by detection of rotavirus in diarrheal stools by ELISA accompanied by a greater than fourfold rise in serum CF and RIA antibody titers to rotavirus. Adults with ~~admitted rotavirus infections were as severely ill as patients with most bacterial enteric infections; only patients with cholera~~ passed more watery stools and were more dehydrated than those with rotavirus infections. Only two of the 28 adults with rotavirus infections had known recent contact with young children with diarrhea. Rotavirus infections in these adults occurred most frequently in the cooler, drier months in Thailand than during the rest of the year. In some settings, rotavirus should be considered in the differential diagnosis of severe diarrhea in adults as well as in young children.

METHODS : Five hundred and twenty six patients over 15 years of age admitted to Bamrasnaradura Hospital, Nonthaburi, Thailand who had passed at least three stools (which assumed the shape of the container) within a 24 hour period for less than 72 hours and had abdominal cramps, vomiting, fever, or prostration were studied. Between October 1, 1980 and September 30, 1981, specimens were collected from each patient on admission, and stool and sera were collected again after three weeks. Plasma specific gravities were determined to assess the degree of dehydration (16). Stools were cultured on selective media and examined for the following accepted or putative enteric pathogens (8); *Salmonella*, *Shigella*, *Campylobacter jejuni*, *Yersinia enterocolitica*, enterotoxigenic *Escherichia coli*, *Aeromonas hydrophila*, *Plesiomonas shigelloides*, and vibrios (including 0-1 and non-01) *Vibrio cholerae*, *Vibrio parahaemolyticus*, and *Vibrio fluvalis*.

Stools were examined for rotavirus by ELISA employing guinea pig and goat antisera to the simian rotavirus, SA-11 virus (2,23). Positive specimens were confirmed by RIA employing both pre and post immunization antisera (2,4). Serum antibodies to rotavirus were determined by complement fixation using SA-11 virus as a substitute antigen for human rotavirus (6) and also by RIA (2,4).

Twenty-eight patients who were not infected with other recognizable enteric pathogens and who were found to be infected with rotavirus by ELISA and also had greater than fourfold rises in antibody titer to SA-11 virus as determined by CF and RIA are the subject of this report. As shown in Table 1, on admission, 57 percent (16/28) of these adults had a complement fixing antibody titer of less than 1:2 to SA-11 virus and 15 percent (4/26) had a titer of less than 1:200 by the more sensitive RIA procedure. Sixty-four percent (18/28) were women between 16 and 72 years of age while ten infected men were between 25 and 52 years of age. Two of 18 women (11%) reported that a family member had also suffered from gastroenteritis within a week of the women's admission and both of family members with diarrhea were children below five years of age. No family members of males with rotavirus diarrhea had previously been ill.

The clinical characteristics of patients with rotavirus infections and of patients infected with other bacterial enteric pathogens are summarized in Table 2. Patients with rotavirus infections were as ill as determined by clinical symptoms, extent of stool purging, and plasma specific gravity as those with *Shigella*, *Salmonella*, *V. parahaemolyticus*, enterotoxigenic *Escherichia coli*, or patients in whom no etiologic agent was found. No attempts were made to identify other causes of viral enteritis, i.e., Norwalk virus, coronavirus, adenovirus, etc. Only individuals with cholera passed more watery stools in a 24 hour period and were more dehydrated (as determined by plasma specific gravity) than adults with rotavirus infections. All 28 patients with rotavirus infections left the hospital within 48 hours after admission and only two continued to pass watery stools for 24 hours after discharge.

As shown in Figure 1, rotavirus infections were found in five percent (28/526) of adults with diarrhea from whom diarrheal stool and acute and convalescent sera were examined. Although fewer cases of diarrhea were admitted to the hospital in the winter months, a higher proportion of them were due to rotavirus. Rotavirus infections were more common in the cooler, drier months of January, February, November, and December than the remaining months of the year (17/124 vs 11/402) ($p < 0.001$).

Diarrhea caused by rotavirus in adults can be severe as exemplified by the 28 patients described in this report. In developed countries 39-63 percent of children hospitalized for acute diarrheal disease are infected with rotavirus (3,12,15) and the prevalence of these infections increases in the cooler months of the year (3,12). In developing countries a similar proportion of children with diarrhea seen at treatment centers are infected with this virus (1,18). There are reports of sporadic outbreaks of rotavirus diarrhea in adults. Ryder et al (19) found that rotavirus was the most frequent etiologic agent among Panamanians with diarrhea visiting Mexico and four of 50 United States soldiers with diarrhea had serological evidence of recent rotavirus infections during their first six weeks in Korea (7). Wenman et al (22) described 43 rotavirus infection in adults in Canada and found most infections were mild and occurred most commonly in adults whose children had rotavirus infections. More recently rotavirus was found in nine percent of 2347 individuals over ten years of age at a treatment center in Bangladesh (1).

It is clear that host factors are important in susceptibility to infections with gastrointestinal pathogens (5). All of the patients with rotavirus infections were in good health prior to admission. Yolken described 13 of 22 immunocompromised patients with a rotavirus infection who died within 11 days of their infection (24). Although an immunological evaluation was not performed, none of the patients with rotavirus infections described in this report had preceding illnesses which would have compromised their immunological defenses and all were well within several days of developing gastrointestinal symptoms.

While intestinal IgA antibody to type specific rotavirus is likely to be important in protection from rotavirus infections, the presence of serum antibody also correlates with resistance to disease in adult volunteers fed rotavirus (13). As in developed countries, systemic complement fixing antibody to either SA-11 virus or Nebraska calf diarrhea virus, two substitute antigens for human rotavirus, is acquired by the majority of Thais by six years of age (9,17). It is not known why some adults are susceptible to rotavirus. Rotavirus type specific intestinal or serum antibody, infecting dose, concomitant disease, as well as undefined host or viral genetic differences involved in primary infection and reinfection may be important. Fifteen percent of adults with rotavirus infections in this report had "acute" serum antibody titers of less than 1:200 as determined by RIA which may partially explain their susceptibility to rotavirus infections. However 25 percent had acute titers that were 1:3200 and these patients still became ill. These individuals may have become infected with serotypes of rotavirus with which they had no previous exposure.

Two of 18 (11%) women with rotavirus infections had young children who also suffered from gastroenteritis; however, none of the ten men or 16 other women with rotavirus infections had known contact with children with gastroenteritis. Rotavirus can be acquired from young children (12,14), but may also be acquired in other settings. Travelers with diarrhea (7,8,19,21) and outbreaks of gastroenteritis in adults (10,11) caused by rotavirus have also been described, implying alternative routes of infection.

Further studies to determine the incidence of type-specific rotavirus infections in adults, especially under conditions where diarrheal disease is endemic, will be required to determine the importance of this viral enteritis in adults. Rotavirus infections in adults can cause diarrhea as severe as most bacterial enteric infections and should be considered in the differential diagnosis of gastroenteritis in adults as well as young children.

Table 1. Rotavirus infections in 28 adults* at Banrasnaradura Hospital

Age	Sex	Antibody titer as determined by CF and RIA			
		Acute		Convalescent	
		CF	RIA	CF	RIA
52	M	<2**	200**	16	>51,200
44	M	2	200	32	51,200
16	F	<2	<200	128	800
26	F	<2	<200	256	>51,200
33	F	<2	800	256	51,200
24	F	2	800	128	12,800
35	M	<2	<200	128	3,200
43	M	16	800	256	>51,200
46	F	2	3,200	256	>51,200
48	F	2	800	512	3,200
36	F	4	3,200	256	12,800
32	F	<2	<200	128	12,800
25	M	8	3,200	256	12,800
27	M	<2	200	256	12,800
41	M	<2	200	128	3,200
23	M	<2	200	256	12,800
72	F	<2	3,200	128	>51,200
49	F	4	3,200	256	51,200
45	F	8	NT	256	NT
23	F	16	NT	256	NT
58	F	<2	800	128	>51,200
26	F	<2	3,200	256	12,800
55	F	<2	800	256	>51,200
32	F	<2	200	64	3,200
38	F	8	800	512	12,800
39	M	8	3,200	64	51,200
54	F	<2	200	256	>51,200
32	M	<2	800	128	12,800

* All patients had rotavirus in their diarrheal stool as determined by ELISA

** Reciprocal of antibody titer

Table 2. Comparison of clinical findings associated with different bacterial pathogens and rotavirus in adults at Bamrasnaradura Hospital

Symptom	% of patients for each pathogen showing symptoms						
	<i>Shigella</i> spp. ^a (82)	<i>Salmonella</i> spp. (12)	<i>V. para-haemolyticus</i> (17)	<i>V. cholerae</i> (26)	<i>Enterotoxigenic E. coli</i> (24)	No enteric pathogen identified (17)	Rotavirus (28)
Headache	72	100	47	61	46	53	79
Anorexia	73	83	47	54	62	65	68
Malaise	82	92	65	69	71	72	71
Nausea	57	75	59	88	71	70	86
Vomiting	45	66	65	85	46	50	61
Chills	80	92	94	27	67	59	68
Tenesmus	95	100	100	65	83	91	96
Fever	83	75	59	23	62	53	61
Sore throat	36	17	12	4	8	10	11
Cough	12	8	12	19	17	14	11
Coryza	10	8	12	4	4	0	0
Stools per 24 h							
≥5	5	8	23	0	12	15	7
5 to 15	78	75	76	42	83	78	68
<15	17	17	0	58	4	7	25
Predominant character of stool							
Watery	6	33	18	88	50	43	61
Mucous	22	50	35	8	33	36	32
Bloody	72	17	47	4	17	21	7
Dehydration ^b	1.0264	1.0283	1.0266	1.0357	1.0275	1.0263	1.0281

^a Number of patients is shown in parentheses.

^b Values show mean plasma specific gravity.

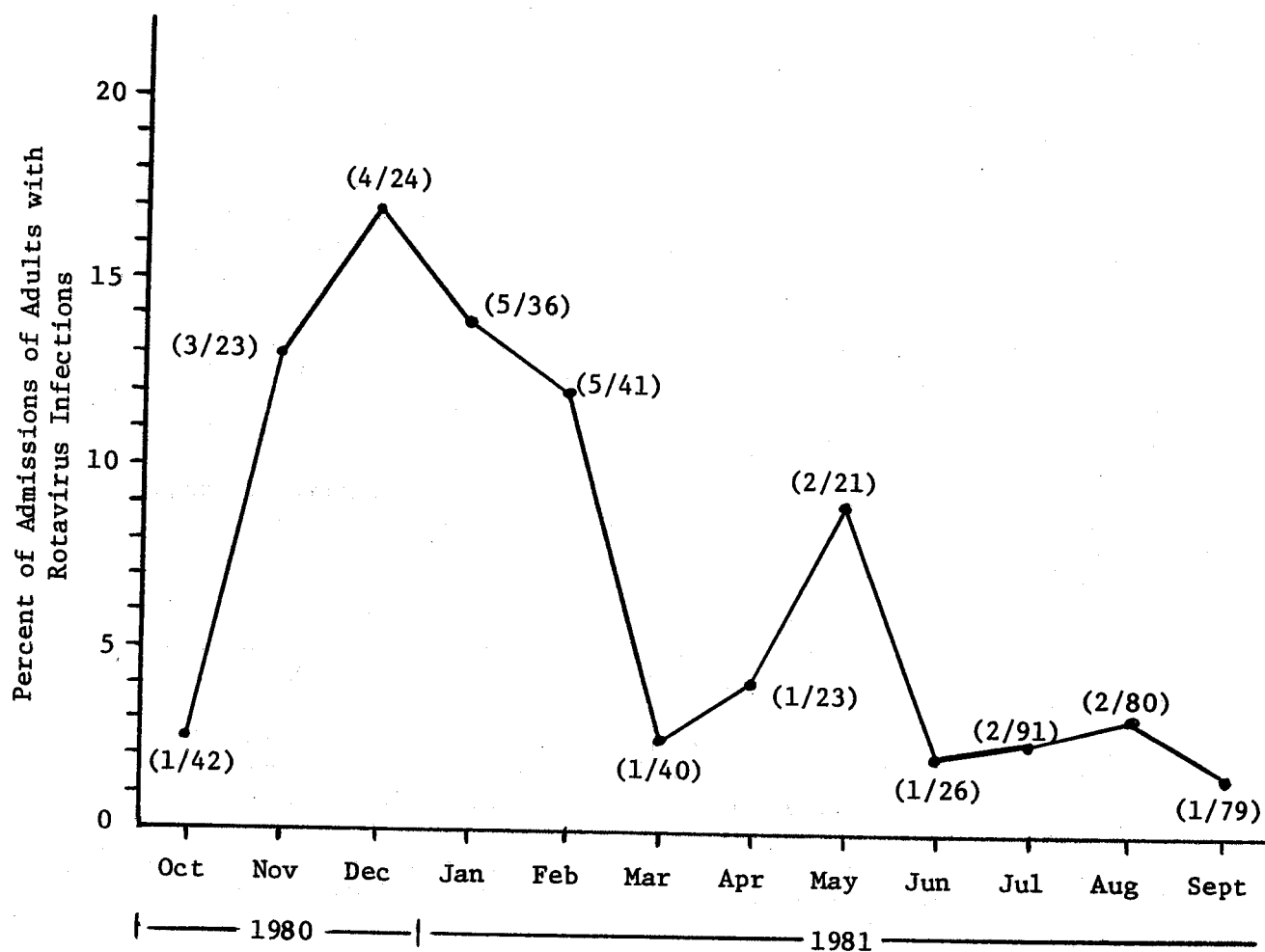


Fig. 1. Percentage of adults with diarrhea due to rotavirus admitted to Bamrasnaradura Hospital between October 1980 and September 1981. Rotavirus infections were determined by the presence of rotavirus in diarrheal stool as detected by enzyme-linked immunosorbent assay accompanied by rises of fourfold or greater in serum CF and RIA antibody titers.

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